REMARKS

The Office Action has been carefully reviewed. No claim is allowed. Claims 8-17 and 21 presently appear in the application and define patentable subject matter warranting their allowance. Reconsideration and allowance are hereby respectfully solicited.

Claims 8-17 and 21 have been rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This rejection is respectfully traversed.

The examiner holds that for the invention to function, it would be required that it be established that increased CD14 be present in the T cells of individuals suffering from any and all types of infections and that CD14 levels are reduced in response to efficacious treatment.

While applicants do not concede that the scope of the invention is not enabled for all types of inventions, in order to expedite prosecution for purposes of business strategy, independent claims 8 and 13 are now amended to be directed to individuals with a high probability of having an HIV infection and to treated HIV-infected individuals, thereby obviating part of this rejection.

With regard to the increased MO2+ cell numbers in both CD4+ and CD8+, the experimental results presented in the executed 1.132 declaration attached hereto clearly demonstrate that MO2+ cell numbers

are significantly increased in both CD4+ and CD8+ cells in Group 1 patients (Table 1).

With regard to the enablement issue on the decrease in MO2+ cell numbers as a measure of the efficacy of the treatment in HIV+ patients, the results shown in Figure 1 of the attached declaration demonstrate that Group 1 patients (in which the anti-HIV treatment was successful) showed a decrease in the percentage of MO2+ CD8+ cells. As a successful anti-HIV treatment from a cellular perspective implies an increase in lymphocyte count, the results for CD4+ cells parallel the results for CD8+ cells. Accordingly, it would be expected by those of skill in the art that there is a decrease in the percentage of MO2+ CD4+ cells, similar to that observed for MO2+ CD8+ cells, as a measure of the efficacy of treatment in HIV+ patients.

Reconsideration and withdrawal of this rejection are therefore respectfully requested.

In view of the above, the claims comply with 35 U.S.C. §112 and define patentable subject matter warranting their allowance. Favorable consideration and early allowance are earnestly urged.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant(s)

By _____
Allen C. Yun
Registration No. 37,971

ACY:pp
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\C\cohn\Tartakovsky1\PTO\amd final OA 4-9-04.doc

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: TARTAKOVSKY=1

In re Application of:	)	Art Unit: 1644
Boris TARTAKOVSKY et al.	)	Examiner: C. R. Ewold
Appln. No.: 09/806,689	)	Washington, D.C.
Filed: July 13, 2001	)	Confirmation No. 5905
For: A NOVEL LYMPHOCYTE POPULATION	)	

DECLARATION UNDER 37 CFR 1.132

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window
Randolph Building, Mail Stop
401 Dulany Street
Alexandria, VA 22314

Sir:

I, Boris Tartakovsky, do hereby state and declare as follows:

I am an inventor of the above-identified application and my educational and professional experience is provided in the CV attached hereto.

The present invention describes the use of an antigen recognized by MO2 monoclonal antibodies in a method for diagnosing in an individual an HIV infection and in a method for monitoring treatment efficacy against HIV infection in HIV-positive individuals. Lymphocytes positive for the antigen are referred to as "*MO2 positive cells*" or "*MO2$^+$ cells*".

It is explicitly stated on page 10, line 1-18 of the present application that the level of MO2$^+$ cells may be used as a marker for monitoring the efficacy of a certain treatment administered to an individual suffering from an infection:

Thus, the level of $MO2^+$ cells in treated infected individual may be used as a basis for determining, on a cellular level, the effect of the treatment on the treated individual. (emphasis added)

The term "*on a cellular level*" in this context should be understood as referring to the correlation between treatment efficacy as demonstrated by cell reconstitution, such as lymphocytes, CD4 and CD8 T cells reconstitution in the patients and percent of MO2-positive cells. This means that a treatment should be considered effective when a decrease in the percent of $MO2^+$ cells, after anti-HIV treatment, is observed.

Support for the above is provided in the experimental results described below and I can attest of my own personal knowledge that all the results reported herein are true and accurate.

Table 1 below shows absolute numbers of different lymphocyte subpopulations previously obtained from five HIV positive individuals, before and after anti-HIV treatment. The values in Table 1 represent the number of different cells: total lymphocytes, CD4 positive and CD8 positive T cells, per micro liter blood before and after treatment.

Table 1: Cellular response to treatment at same time

Patient no.		Lymphocytes		CD4		CD8	
		Pre	Post	Pre	Post	Pre	Post
Group1	1	400	1400	44	272	222	805
	2	1000	1700	100	258	706	959
	5	700	1200	55	146	405	666
Group2	3	2400	1500	420	435	1027	609
	4	2100	2100	286	313	1224	1155

Pre = before treatment
Post = 1-3 months following treatment initiation (HAART)

It is known that HIV positive individuals suffer from a decrease in their lymphocyte counts, especially of CD4 positive T cells. A successful treatment, from the cellular aspect, implies that an increase in lymphocyte count be obtained. Examining this effect on HIV patients before and after anti-HIV treatment demonstrated that this improvement was

achieved only in one group (Group 1) of patients but not in the other group of patients (Group 2), as shown in Table 1.

This improvement correlated with the percent of $MO2^+$ cells in the samples obtained from each patient, which was also examined and which is also shown in the Figure 1 attached hereto. Specifically, patients 1, 2, and 5 (Group 1) exhibited a decrease in the percent of $MO2^+$ cells (as an example of MO2 positive cells, CD8 positive T cells are shown in the Figure, but the same results were obtained when testing for MO2 positive CD4 positive T cells or for MO2 positive CD3 positive cells), to levels comparable to the percent levels observed in healthy individuals. Patients 3 and 4 did not exhibit a decrease in the number of $MO2^+$ cells.

It is thus evident from Table 1 and from Figure 1 attached hereto that for patients exhibiting a decrease in the number of $MO2^+$ cells (Group 1, patients number 1,2 and 5) a significant cellular reconstitution took place while patients which did not show a decrease in $MO2^+$, also did not show cellular reconstitution (Group 2, patients number 3 and 4).

Thus, as also concluded in the present application at the time the invention was made (e.g., at page 10, lines 1-18), the percent of $MO2^+$ cells in HIV patients undergoing treatment can be used as a marker of cellular reconstitution. Cellular reconstitution is a sign of the effectiveness of treatment from the cellular aspect.

I hereby further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 81 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon:

Boris Tartakovsky — April 14, 2005
Date

G:\BN\C\cohn\Tartakovsky1\updated DraftDeclaration.Doc

01320993\55-01

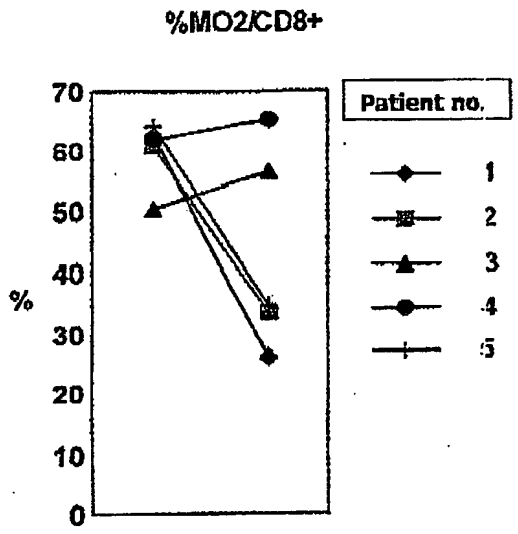

Figure 1

Five HIV patients were tested for %CD8+MO2+ cells before (left) and 1-3 months after (right) treatment (HAART) initiation.
As shown, three patients respond to treatment by decreasing MO2 levels (patients no. 1, 2 and 5; designated above as group 1) whereas two others did not (patients 3 and 4; designated above as group 2).

Curriculum Vitae

Boris Tartakovsky

Address: 4, Zilberman St.; Rehovot; 76656; Israel
Mobile phone: 054 7619610
Email: b.tartakovsky@medscape.com; boris.tartakovsky@gmail.com

Vast experience in both academic, clinicallly oriented scientific research and in industrial research and development, product development and business development. Proven experience in senior executive positions in various companies. Extensive experience in evaluation of projects, in due diligences of companies, in organising, instructing and supervising of R&D groups and initiating collaborations with other companies.

Professional Experience

June 1996-Present: Consultant in Biotechnology (Novamed, MDR-tests, Compugen, Orgenics, Teva, more). Planning of projects, R&D organization, evaluation of projects and manpower, writing of opinions (scientific, market needs, directions) for Israeli and foreign companies, due diligences of companies in Israel and abroad, technological advisor in product development, supervision and follow up of projects. Expertise in Immunology, Cell Biology, Infectious Diseases.

August 2003-Present: Senior Investigator, The Hematology Institute, Tel Aviv Medical Center. The research focuses on a novel cellular marker, discovered originally by myself, and its value in hemopoietic stem cell transplantation.

June 2001- May 2002: Chief Scientific Officer, Mindsense Biosystems.
In house supervision of R&D activities; Collaborations with other companies and Scientific Business Development (Ciphergen biosystems US, Hybrigenics France, more). The Company was developing under my direction and supervision a multimarker diagnostic procedure for Major Depression. The methodology is based on the concomitant analysis of intracellular proteins by FACS. In addition, I have collaborated with Ciphergen Biosystems in the development of a multimarker test, for Major Depression, based on plasma protein detection and quantitation using protein chips, mass spectrometry and novel multimarker analysis software (see patent applications).

Contacts with other US companies such as Genomic Solutions, Incyte Genomics, Affymetrix, Intrinsic Bioprobes.

May 2000- May 2001: VP Science&Technology, Mindsense Biosystems.
Have successfully redirected and recreated the whole scientific basis of the company. Have organised and supervised the R&D group. Have initiated collaborations with other Companies in Israel and abroad.

September 1999- April 2000: Consultant, Mindsense Biosystems.
Have introduced flow cytometry and intracellular macromolecule detection to Company. Have demonstrated and proven that acquired, licenced technology was unsound.

June 1996-December 2001: Founder and Head, Research Unit, in The Clinical Immunology and AIDS Center, Tel-Aviv Medical Center.
The unit, affiliated to the Tel Aviv University Medical School concentrated on HIV research. The focus was on chemokines (see list of publications, upon request) and later, on my discovery of a novel population of lymphocytes in human peripheral blood, expressing an intracellular CD14-like antigen (see list of publications, upon request and patent applications).

1995-May 1996: R&D Director, Savyon Diagnostics and R&D Director, Healthcare Technologies, Ltd.
Numerous diagnostic kits, based on different platform technologies, have been developed, produced in house and marketed. The main focus of the Companies was infectious diseases, especially Chlamydia trachomatis, Chlamydia pneumonia (and means to avoid cross reaction in diagnosis), Urinary Track Infections and HIV.

1994-1995: R&D Director, Savyon Diagnostics, Ltd.

1993-1994: Sabbatical Leave from Weizmann Institute of Sciences; Research & Development Manager, Savyon Diagnostics, Ltd. Organised and headed a new R&D group and new laboratories.

Education

Oct 1988-Sep 1994: Senior Scientist, Department of Chemical Immunology, The Weizmann Institute of Science, Rehovot, Israel.

Most of my independent academic career focused on immunology of reproduction. I have established in vivo models of abortions and of mal-implantations, based mainly on cytokines such as CSF1, TNF and others such as anti cardiolipin antibodies. I have demonstrated in animal models that cytokines and anticardiolipin antibody- associated pregnancy failures stem from defectice implantation problems (published in Dev Biology, Biol of Reprod and PNAS- see these and others in list of publications, upon request).

In addition, I have established together with R. Romero an in vivo system of premature delivery based on Interleukin 1 and its receptor antagonist (see list of publications, upon request); and also have elucidated the molecular mechanism of action of methotrexate in Rheumatoid Arthritis (see publication list, upon request).

These in vivo models have provided important functional insight into complex cellular and molecular normal and pathological situations in humans.

August 1986-Sep 1988: Scientist, Department of Chemical Immunology, The Weizmann Institute of Science, Rehovot, Israel.

Aug 1984-July 1986: Visiting Fellow, National Institute of Health, National Cancer Institute, Laboratory of Molecular Immunoregulation, MD, USA. Chief: Dr. J.J. Oppenheim.

Aug 1983-July 1984: Postdoctoral fellow in the Department of Pathology, Division of Immunology, Yale University School of Medicine, New Haven, CT, USA. Advisor: Prof. C.A. Janeway.

Aug 1982-July 1983: Postdoctoral fellow in the Department of Pathology, Division of Immunology, Yale University School of Medicine, New Haven, CT, USA. Advisor: Prof. R.K. Gershon. (deceased July 1983).

June 1983: Ph.D. awarded

1978-1982: Ph.D., Faculty of Life Sciences, Feinberg Graduate School of the Weizmann Institute of Science. Title of Thesis: "Sex-Associated Differences in the Regulation of Immune Processes" Under the guidance of Prof. S. Segal, Department of Cell Biology at The Weizmann Institute of Science, Rehovot, Israel.

1975-1977: M.Sc., Faculty of Life Sciences, Feinberg Graduate School of The Weizmann Institute of Science. Title of Thesis: "Segregation of immune characteristics of subpopulations of peripheral blood-derived T lymphocytes in healthy and autoimmune-diseased subjects". Under the guidance of Prof. S. Segal, Department of Cell Biology at The Weizmann Institute of Science, Rehovot, Israel.

1971-1974: B.Sc., Faculty of Life Sciences, University of Tel-Aviv. Major: Biology

Technologies

Vast Experience: ELISA, Rapid ELISA, Solid Phase Enzymatic Reactions, Immunodominant peptide-based ELISA, Dot Blot, Flow- Through Membrane, Lateral Flow Membrane, ImmunoGold, Immunofluorescence, TRF, Flow Cytometry, Intracellular Staining, FACS analysis, Cellular Assays, Cell Activation, Apoptosis, more.

Experience: Biosensors, ProteinChips, Western Blot, Mass Spectrometry, DNA Chips, PCR, InSitu Hybridization, Northern Blot, more.

Academic Awards

1982-1984: The Chaim Weizmann Postdoctoral Fellowship.

1984-1986: NIH Visiting Program Award.

1986-1987: The Lalor Foundation Research Grant Award on Mammalian Reproductive Physiology.

1987-1988: Incumbent of the Aser Rothstein Career Development Chair in Genetic Diseases.

1988-1991: Incumbent, Yigal Allon Fellowship.

Scientific Associations

1988-1993: Secretary-Treasurer, The Israeli Society of Reproductive Immunology.

1990-Present: Member, The Israeli Society of Immunology.

1991-Present: Member, The American Society for the Study of Reproduction.

1994-Present: Member, The Israeli Society of Microbiology.

1995-Present: Member, The American Society of Microbiology

Research Interests

1. Immunology and Diagnostics of Infectious Diseases.
2. Phospholipids as Immunogens and Antigens.
3. Nutritional Modulation of the Anti-Phospholipid Immune Response.
4. Regulation of T cell Functions by Cytokines.
5. Immunobiology of Pregnancy and Embryonic Implantation.
6. Chemokines and HIV Disease Progression.
7. Intracellular Markers of Lymphocyte Activation and Apoptosis.
8. Biomarkers of Mental Disorders.

Academic Grants

1986-1987: Lalor Foundation. The Induction of Immune-mediated Abortions in mice.

1988-1991: German-Israeli Foundation for Scientific Research and Development (GIF). Lymphokines and Autoimmunity.

1989-1992: The Israel Academy of Sciences and Humanities. The Common Biology of Embryo and Tumor Development: Immunoregulation and Growth Factors.

1991-1993: German-Israeli Foundation for Scientific Research and Development (GIF). Cytokines and Autoimmunity.

1994-1996: Savyon Diagnostics. Development of Diagnostic Tools for the Evaluation of Pathogenic Anti-phospholipid Antibodies. In collaboration with E. Mozes, The Weizmann Institute of Science.

2003-2004: Novamed. The MO2 antigen in hemopoietic stem cell transplantation

Patent Applications

1. "A Novel Lymphocyte Population" (Tel Aviv Medical Center).

2. "Methods and Compositions for Diagnosing and Treating a Subject Having Depression" (Mindsense Biosystems).

3. "Depression Biomarkers and Methods for Detecting and Diagnosing Depression" (Mindsense Biosystems).

4. "Methods of Diagnosing a Subject Having Depressive Disorder " (Mindsense Biosystems).

Teaching Positions

1987: WHO and ICRO-UNESCO International Course in Immunology. The Weizmann Institute of Science, Rehovot, Israel.

1990: International Laboratory Training Course on Molecular and Cellular Aspects of Immunology. The Weizmann Institute of Science, Rehovot, Israel.

1990-1991: Seminar on Autoimmunity and the Biology of Cytokines. The Weizmann Institute of Science, Rehovot, Israel.

1996-2000: "Introduction to Chemistry and Microbiology of Food and Nutrition". Ben-Gurion University, Beer Sheva, Israel.

1998-2002: Bar-Ilan University, Ramat Gan, Israel.
Deliver Lectures on "Immunopathology" and in "Special Subjects in Virology and Immunology":

▶ Innate Immunity.

▶ Chemokines as Immune Weapons.

▶ Chemokine and Chemokine Receptor Involvement in the Pathogenesis of HIV.

▶ Viral Mechanisms of Immune Evasion.

2005- "Introduction to Chemistry and Microbiology of Food and Nutrition". Ben-Gurion University, Eilat Campus.

Invited Lectures to National and International Conferences

1. International Symposium on Immunology of Reproduction. Tel-Aviv, Israel, October 21-25, 1984. "Induction of abortions in mice by immunization against fetal or tumor antigens."

2. Second Banff Conference on Reproductive Immunology. Banff, Canada, February 15-18, 1985. "The induction of immune-mediated abortions in mice: a unique approach."

3. INSERM Colloquium on Immunology of Reproduction. Paris, France, December 3-6, 1986. "Murine models of immunologically induced abortions."

4. International Meeting on Pregnancy Loss. Tel Aviv, April 9-12, 1989. "Modulation of pregnancy induced by a tumor cell line."

5. Molecular and Cellular Immunology of the feto-maternal relationship. INSERM Coloquium. December 1990, Paris, France. "Cytokines as modulators of early embryonic development."

6. XVIth Symposium Strasbourg-Weizmann on Molecular Immunology. Rehovot August 1991. "Immunomodulation of embryonic development, implantation and pregnancy."

7. International Conference on Rheumatic Diseases in Pregnancy. Jerusalem May 1992. "Early pregnancy loss: Role of cytokines in implantation and possible implications in SLE and APS."

8. Annual Meeting of the Israeli Society of Immunology, Bar-Ilan University, June 1992. "Immunology of Pregnancy: old ideas and new concepts."

9. Annual Meeting of the Israeli Society for Immunology of Reproduction, March 4, 1993, Tel Aviv University. "Immunomodulating Cytokines in Pregnancy."

10. Third G.I.F. Meeting on Cancer and Immunopathology, March 21- 24, 1993, Dead Sea, Israel. " Cytokines and Autoimmunity."

11. The Jerusalem AIDS Conference, December 4, 1996, Jerusalem. "Intracellular Expression of MIP1 beta in HIV-Infected Patients."

12. Invited Participant: Press Lunch on "Chemokines, correlation of protection and some biological approaches to prevention and therapy". With R. Gallo, A. Fauci, A. DeVico, G. Biberfeld, D. Bolognesi, T. Shall, N. Landau. 1998 Annual Meeting of the Institute of Human Virology, Baltimore, August 1998.

13. Clinical Applications of Flow Cytometry, Towards the New Millennium. June 20, 1999, Tel- Hashomer, "Intracellular Staining of Chemokines and AIDS Development".

14. First International Workshop on HIV Pathogenesis, March 26-28, 2000, Dead Sea, Israel. " CD14-like Antigen as a Marker for HIV Disease".

15. "A Novel Lymphocyte Subpopulation", August 3, 2004, Charite, Berlin.

Ad Hoc Academic Reviewer (last three years)

International Journals

Cytokines
Eur. J. Clin. Invest.
Cytometry

Research Grant Foundations

German-Israeli Foundation
Israel Academy of Sciences
Israeli Ministry of Health
Binational Science Foundation

Supervision of Students and Medical Doctors

1. 4 M.Sc. Students at the Weizmann Institute of Science

2. 2 Ph.D. Students at the Weizmann Institute of Science

3. 2 M.Sc. Students at Tel-Aviv Medical Center

4. 5 M.D's at the Weizmann Institute of Science

5. 6 M.D's at Tel-Aviv Medical Center

Publications

More than 65 publications. Last one published November 2004.